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Original Communication

Forensic issues in Down syndrome fatalities

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Abstract

Down syndrome, or trisomy 21, is the most common chromosomal abnormality associated with intellectual impairment. Premature death is a feature of the syndrome due to a wide variety of conditions including congenital heart disease, impaired immune responses resulting in respiratory infections, acute leukaemia, upper airway narrowing, pulmonary hypertension, Alzheimer disease and atlanto-axial instability. Cases of Down syndrome not uncommonly present for medicolegal autopsy, as the non-specificity of symptoms and signs often precludes accurate antemortem establishment of a cause of death. Manifestations of Down syndrome are reviewed with an analysis of possible mechanisms of death and findings at autopsy.

Keywords: Down syndrome; Autopsy; Sudden death

1. Introduction

Down syndrome was first described by Down in 1866 and linked to trisomy 21 in 1959 by Lejeune and Jacobs. It is the most common chromosomal abnormality causing intellectual disability with intelligence quotients (IQs) in the range of 20–85. There is no racial predilection, the male to female ratio is approximately 1.15:1, and it occurs in approximately 1 in 500 to 1 in 1000 live births.[1] Advanced maternal age is a risk factor. As well as intellectual impairment, manifestations include a variety of congenital malformations. In forensic practice, cases of Down syndrome may present considerable difficulties, as manifestations may be quite diverse and involve many organ systems, and detailed clinical histories are usually lacking. There are also a number of potential causes of unexpected death. The following review details possible findings at autopsy in cases of Down syndrome that may not be associated with the fatal episode, or that may relate directly to death. Possible mechanisms of death and considerations at autopsy are discussed. Although primarily focussed at the paediatric age group, all ages have been included for completeness of the review.

2. Discussion

2.1. Background

There is an increased mortality rate at all ages in Down syndrome. Intra-uterine deaths occur with elective terminations, or from spontaneous abortions due to the often ill-understood effects of congenital defects. It has been estimated that the age-adjusted mortality for those with the syndrome is 5.4 times that of the general population, with the highest mortality ratio (13 times) in the age range one to four years.[2] This stabilises to between 3.5 and 4.7 times, with an accelerated death rate after 35 years of age, reaching 10.1 times that of the general population between 55 and 64 years.[2,3] Down syndrome is also associated with premature aging.[4]

One of the difficulties in reviewing the literature on medical and surgical emergencies and sudden, unexpected death in Down syndrome is that many studies have analysed these problems in intellectually disabled individuals as a group without describing the specific situation for

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Down syndrome.[5,6] (This may explain some of the contradictory conclusions that have been reported.) For this reason, the following analysis will sometimes deal with the broader range of individuals with intellectual and developmental disabilities. Intellectual disability has been defined as significant below-average intellectual functioning before the age of 18 years combined with relative limitations in two or more adaptive skills in the areas of self-care, communication, social skills, home living, academic skills, use of community resources, leisure and work, and health and safety.[6] In addition, papers do not always detail specific age ranges when describing conditions, and so all age ranges have been included in this overview.

Although Down syndrome patients have higher mortality rates than the general population, this has improved in recent years due to better diagnostic and therapeutic modalities, as well as to improvements in living conditions and physical care.[2,7–9] This has resulted in fewer deaths due to infections.[10] There have also been advances in cardiac surgery that have improved survival for those with significant congenital cardiac defects.[11] For example, the percentage of survivors to one year and 10 years over the period 1944–1955 was 47% and 37% respectively, compared to 94% and 86% over the period 1966–1975.[11] The average life expectancy in 1929 of nine years contrasts with survival of 61% of affected individuals to the age of 50 years in 1987.[1]

2.2. Genetic basis

The manifestations of Down syndrome result from an extra copy of the proximal part of 21q22.[12] Congenital cardiac defects are associated with the 21q22.1-q22.3 region, or Down syndrome critical region [DSCR), and DSCR1 at 21q22.1-q22.2 is involved with intellectual impairment and/or cardiac defects.

2.3. Morphological features

2.3.1. External

Typical features in an individual with Down syndrome include short stature and obesity with a small, rounded head (microcephaly and brachycephaly), a flattened occiput, and a sloping forehead. In infants the fontanelles are large and slow in closing. Radiologic examination may reveal hypoplasia of the maxillary sinuses and absence of the sphenoidal and frontal sinuses. The nasal bones are hypoplastic with a flattened nasal bridge.[12]

The face is characteristic, with a rounded shape, an open mouth with protruding tongue, angular cheilitis, and chapping of the lower lip. The tongue is fissured and the teeth may be malformed, malocclusion, absent or small. Supernumerary teeth and hypocalcification occur.[12] The eyes have a variety of abnormalities including upwardly slanting palpebral fissures, bilateral epicanthic folds, Brushfield spots and cataracts. The ears are often small with overfolding of the helix. There may be evidence of chronic otitis media. Scalp hair is sparse with partial or total alopecia often occurring after puberty, and sometimes in childhood.[4]

The chest may show close spacing of the nipples and there may be an umbilical hernia of the abdominal wall. Male genitalia may be small with hypospadius and cryptorchidism. The hands tend to be short and broad with clinodactly of the little fingers and a single flexion crease in 20% of individuals. The big and index toes are often widely spaced. A variety of skin lesions may occur, including alopecia areata, vitiligo, xerosis, focal hyperkeratotic lesions, elastosis serpiginosa and recurrent abscesses and skin infections. Muscular hypotonia may have been noted during life.[4]

2.3.2. Internal

Congenital cardiac defects are often encountered in Down syndrome and are reported in 19–43% of cases.[11,12] The most common lesion is an endocardial cushion defect in 43% of cases, followed by ventricular septal defect (32%), atrial septal defect (10%), tetralogy of Fallot (6%) and isolated patent ductus arteriosus (4%). Approximately one third of cases have multiple defects. Seventy percent of individuals with an endocardial cushion defect have Down syndrome. There may be evidence of right ventricular hypertrophy as a manifestation of cor pulmonale from pulmonary hypertension, the aetiology of which may be due to the combined effects of hypoxia from upper airway narrowing with significant sleep apnoea, and hypoxaemia due to shunt reversal with certain congenital cardiac defects.

Examination of the upper aerodigestive tract may reveal luminal narrowing with enlargement of the tonsils and adenoids, lingual tonsils, choanal stenosis, glossoptosis and subglottic stenosis. Associated abnormalities of the gastrointestinal tract in the young include oesophageal atresia with or without a tracheo-oesophageal fistula, Hirshprung disease and duodenal atresia.

Instability of the atlanto-occipital joint that is found in 14% of cases due to laxity of the transverse ligaments may have resulted in compression of the underlying spinal cord. Accelerated age-related changes may be found with the early development of Alzheimers type dementia and degenerative vascular disease.

Other major congenital abnormalities that have been found in 5.5% of cases have included hypospadius, urethroperitoneal fistula, cleft palate, Meckel diverticulum, cataract, optic atrophy and vascular rings. Minor congenital defects also present in 5.5% of cases include syndactyly, inguinal hernia, undescended testis, urinary bladder diverticulum, and hip and patellar dislocation.[1] None of the latter abnormalities have an effect on mortality.

Histologic examination of other tissues may confirm the presence of pulmonary hypertensive changes in the lungs, and reveal fibrointimal hyperplasia of the vasculature. Leukaemia may be manifested by splenomegaly and lymphadenopathy, and can be confirmed histologically. Although it has been suggested that a variety of other tumors have an increased incidence in adults with Down syndrome, a study

of 793 cases taken from national mortality data in the United States showed only an increased death rate from haematopoetic tumors, with reduced rates of gut, breast and genital organ tumors.[10] Lower rates of solid tumors have also been reported by other investigators, except for testicular and ovarian tumors, and retinoblastoma.[13–15] However, in a study of 4872 individuals with Down syndrome from Sweden and Denmark an increased incidence of testicular, penile and liver cancer with an elevated mortality from stomach cancer was documented,[16] raising the possibility of variations in manifestations between different communities (although selection bias was also raised as a possibility by the authors, given that their cases were taken from hospital registers).[16] The increased numbers of testicular tumors may be associated with the higher rate of undescended testes.[16] Hypogonadism is a feature with ovarian hypoplasia.[4] Histologic abnormalities of the thymus gland include marked enlargement of Hassall's corpuscles associated with precocious thymic involution.[4,17]

A variety of haematologic abnormalities have been documented in Down syndrome including an increased rate of leukaemoid reactions (high leukocyte counts mimicking acute myeloid leukaemia in response to stress or infection), neonatal polycythaemia, thrombocytopaenia and abnormal polymorphonuclear leukocyte lobe counts and decreased granulocytic precursor cells.[10] These may have been demonstrated on antemortem blood films. Typical morphologic features are summarised in Table 1.

2.4. Mechanisms of death

As elective termination is now widespread with increased accuracy and use of antenatal screening, up to 75% of Down syndrome cases die before birth. Following birth, problems may arise in the diagnosis of acute medical and surgical conditions in intellectually disabled individuals, such as those with Down syndrome, as there may be problems with communication, altered reaction to pain, sensory and motor impairment, abnormal behaviour and coexisting medical conditions and congenital anomalies.[6] Histories of illness may therefore be quite short (<24 h) and sudden collapse may be the first indication of problems.[5]

Deaths in Down syndrome individuals may be related to the underlying syndrome or may be entirely coincidental. Traumatic deaths may be due to inflicted trauma or to accidents. Suicides in Down syndrome individuals appear rare[18] and deaths due to violence or accidents tend to be less common than in the general population,[10] although severe mental and physical impairment may make children vulnerable to sleeping accidents and suffocation.[19] Although it has been claimed that a diagnosis of SIDS can be made in individuals with Down syndrome[1] this would not be usual practice, as the presence of a significant abnormality (e.g. trisomy 21) should preclude the use of this term.[20,21] Lethal natural diseases involve a range of different organ systems and may cause sudden and unexpected death.

2.4.1. Cardiac

Congenital cardiac defects are present in nearly half of the children with Down syndrome and are a well-recognised cause of death, particularly at young ages.[1,2] As noted above, the most common defect is an endocardial cushion defect (complete atrioventricular septal defect) occurring in 42.1% of cases in the series of Frid et al.,[1] with primary atrial septal defect, ventricular septal defect, secondary atrial septal defect, tetralogy of Fallot, patent ductus arteriosus, coarctation of the aorta, single ventricle, anomalous

Table 1
Morphological findings in Down syndrome

External	
General	Short stature, obesity
Head and Neck	Microcephaly, brachycephaly, sloping forehead, flattened occiput, large fontanelles, hypoplastic/absent nasal bones with flattened nasal bridge, round face, protruding and fissured tongue, angular cheilitis, malformed teeth, epicanthic folds, upward slanting palpebral fissures, Brushfield spots, cataracts, sparse hair/alopecia, small ears, overfolding of helix
Trunk	Closely spaced nipples, umbilical hernia, inguinal hernia, hypospadius, cryptorchidism, urethroperitoneal fistula,
Limbs	Short and broad hands, clinodactyly, syndactyly, wide space between big and index toes, single flexion crease
Skin	Alopecia areata, vitiligo, xerosis, elastosis serpiginosa, abscesses
Internal	
Upper airway	Enlarged adenoids/tonsils, lingual tonsils, choanal stenosis, glossoptosis, cleft palate, subglottic stenosis, tracheo-oesophageal fistula
Heart	Endocardial cushion defect, ventricular septal defect, atrial septal defect, tetralogy of Fallot, patent ductus arteriosus, right ventricular hypertrophy (cor pulmonale),
Vessels	Pulmonary hypertension, fibrointimal hyperplasia, vascular rings
Eyes	Optic atrophy, cataracts, retinoblastoma
Ears	Otitis media
Skeleton	Instability of atlanto-occipital joint, hip and patellar dislocation, hypoplasia of maxillary, sphenoidal and frontal sinuses,
Gut	Oesophageal atresia, tracheo-oesophageal fistula, duodenal atresia, Meckel diverticulum, Hirschprung disease, liver cancer, stomach cancer
Genitalia/bladder	Bladder diverticulum, testicular and penile cancer, ovarian hypoplasia
Brain	Alzheimer disease
Haematopoetic system	Leukaemia with lymphadenopathy and splenomegaly, precocious thymic involution

pulmonary veins, pulmonary valve stenosis, mitral stenosis, cor triatriatum and right ventricular hypoplasia also occurring. Transposition is extremely rare in Down syndrome.[1] Despite premature aging, fewer deaths were attributed to ischaemic heart disease in Down syndrome than in the general population by Scoll et al.[10] contrasting with the study by Hill et al.[16] where there was an increase in mortality due to ischaemic heart disease.

2.4.2. Vascular

Pulmonary hypertension may develop in children with congenital cardiac defects in Down syndrome at an early age[1] associated with hypoxia from airway narrowing and cardiopulmonary disease, and increased pulmonary artery pressures from shunting through septal defects. Cor pulmonale with right ventricular hypertrophy may result in lethal arrhythmias.[20]

A case has been reported of fatal haemorrhage from a vascular malformation of the lungs in a boy with Down syndrome who had evidence of previous episodes of bleeding.[22] Fibrointimal hyperplasia of vessels and intracerebral vascular changes of Moyamoya disease have also been documented in Down syndrome.

Pulmonary embolism is an uncommon cause of death in Down syndrome but may be associated with congenital cardiac anomalies such as pulmonary stenosis and septal defects. Deep venous thromboses have been found in individuals with mental retardation who have not been mobilising, and fat embolism has been described following femoral fracture in older individuals.[23] Rarely, fatal coronary artery embolism with myocardial infarction may occur in Down syndrome.[24]

2.4.3. Endocrine

An increased incidence of diabetes mellitus has been demonstrated in Down syndrome between the ages of 24 and 34 years[10] and deaths have been ascribed to diabetes and to hypothyroidism.[8] A tenfold increase in mortality from diabetes mellitus was reported in a cohort study of 1425 cases of Down syndrome from institutes in the United Kingdom, possibly associated with nephropathy and renal failure.[15] The age of onset of diabetes may be younger than the general population.[16] Hypothyroidism has been reported in 20–40% of Down syndrome cases associated with the presence of antithyroid antibodies.[12]

2.4.4. Infectious

Down syndrome individuals have a higher rate of infections, particularly of the respiratory tract, than the general population, with bronchopneumonia being a common cause of death at older ages.[2] Increased mortality due to infection has, however, been documented at all ages,[10] with a 50 times incidence of infection and a mortality rate 124 times that of the general population.[4] Increased infections have been attributed to a variety of factors including environmental exposure to pathogens in institutions, reduced mobility, congenital heart disease, abnormal pulmonary vasculature and abnormal immunological function (The latter exacerbated by age).[11,25] More serious respiratory infections tend to occur in the more profoundly intellectually impaired.[26,27] An increased rate of Hepatitis B infection has been found that may result in an increased mortality from liver cirrhosis and liver cancer.[16]

2.4.5. Immunological

Infections result in part from an abnormal immune system. While the aetiology of the proposed abnormal humeral and cell-mediated immunological function in Down syndrome remains unclear, with inconsistent results being found,[10] defects have been demonstrated in B, T and natural killer cell function, in cytokine production, in phagocytic and chemotactic responses, and in immunoglobulin levels with reduced levels of lymphocytes.[12,16] Impaired T cell function is associated with low CD4 numbers. Autoimmune disease occurs with anti-thyroid, antigliadin and anticardiolipin antibodies and worsening immunoglobulin function with age.[4,17]

2.5. Central nervous system

Down syndrome individuals have an increased rate of Alzheimer-type changes in the brain with an increased risk of stroke,[11] the latter associated with the presence of antiphospholipid antibodies.[17] Cerebrovascular haemorrhage may also be associated with increased production of β-amyloid protein associated with the chromosome 21 APP gene, so called cerebral amyloid angiopathy.[16] Alzheimer type changes develop at an earlier age in Down syndrome associated with premature aging and histologic evaluation of older brains may show neurofibrillary tangles, senile plaques and granulovacuolar degeneration.[4] The increased mortality rate in Down syndrome individuals after the age of 35 years compared to individuals with other causes of intellectual disability has been attributed to the effects of early dementia,[28] with the mean age of death in Down syndrome being six years less than in other patients with mental impairment.[29] The development of dementia may be heralded by problems with swallowing, frequent choking and aspiration pneumonia.

Epileptic seizures may also occur, however, although epilepsy is recognised as a cause of an increased rate of sudden and unexpected death in intellectually impaired individuals,[30] its significance in Down syndrome may vary with age. Epilepsy has been described as not a common finding in Down syndrome and rarely documented as a cause of death in some studies,[23] contrasting with others who have found a high prevalence of epilepsy (8–17%) with an associated elevated mortality rate.[16] It appears that seizures occur in 5–7% of Down syndrome children, compared to 20–50% of children with other forms of mental impairment, but are found at a higher rate in adult Down syndrome individuals with dementia compared to those with Alzheimers disease in the general population.[12] Risk factors for death related to epilepsy in adults with intellec-

tual impairment have included non-ambulatory status and poorly controlled seizures.[30]

Congenital central nervous system anomalies such as hydrocephalus and anencephaly have not necessarily been found to be increased in Down syndrome.[10]

2.5.1. Skeletal

Although the symptoms and signs of atlantoaxial instability are usually chronic, resulting from compression of the cord and'/or nerve roots, lethal respiratory arrest may occur from acute compression of the upper cervical cord.[12] The most common cause of atlantoaxial instability in Down syndrome is laxity of the posterior transverse ligament, sometimes associated with malformation of the odontoid. Atlantoaxial instability has been reported in 8.5–40% of individuals with Down syndrome[31–33] and is something to consider at autopsy if the cause of death is unclear.

2.5.2. Haematopoetic

There is a 14–22 times increase in the rate of leukaemia in Down syndrome. The predominant types are acute lymphocytic and acute myeloid leukaemia, with acute megaloblastic leukaemia as the main subtype, although the clinical and biological manifestations may be different to non-Down children. Down syndrome children under the age of four years have a 100 times increase in the occurrence of acute myeloid leukaemia.[34] In addition, an increased rate of other haematopoetic malignancies has also been reported.[10,11]

2.5.3. Respiratory

Upper airway narrowing in Down syndrome has resulted from a range of conditions including midface hypoplasia, macroglossia, narrowing of the nasopharynx, tonsillar and adenoidal enlargement, lingual tonsils, choanal stenosis, shortening of the palate and glossoptosis. In addition subglottic stenosis, laryngomalacia, tracheomalacia and congenital malformations of the larynx, trachea and bronchi may also further reduce the diameter of the airways.[35] Exacerbating factors including obesity and gastro-oesophageal reflux may contribute to the occurrence of sleep apnoea.[10,36]

Asphyxial deaths have been reported in mentally handicapped individuals from a combination of factors including respiratory depression from major tranquillizers, autonomic instability and impaired swallowing reflexes. Bulimia and eating disorders may also predispose to food asphyxia,[23] however it is unclear whether these factors are significant in the subpopulation of those with Down syndrome. Bronchopneumonia and aspiration pneumonia may be causes of death.

2.5.4. Gastrointestinal

A range of gastrointestinal conditions and problems may be fatal in individuals with mental impairment as victims may not be able to clearly articulate their symptoms. Abdominal distension, prolonged constipation, anorexia, vomiting, fever and increasing irritability have all been noted as potentially significant prodromal features,[6] although these may not always occur.[5] Congenital gastrointestinal tract malformations have been documented in 7.3–11% of cases of Down syndrome and are associated with a high mortality rate, particularly if there are concomitant cardiac malformations.[1,37] Congenital gastrointestinal defects include: tracheo-oesophageal fistula/oesophageal stenosis/atresia, pyloric stenosis, duodenal atresia/obstruction, annular pancreas, bile duct atresia, hypoplasia of the small intestine, malrotation, Hirschprung disease and imperforate anus. Gastro-oesophageal reflux is not uncommon, and duodenal ulcer, gallstones and hepatitis B infection have all been reported.[1,37]

Gastric perforation has been reported from viscus distension secondary to aerophagia, defective autonomic control and skeletal deformity in other severely disabled individuals.[38] Hypotonia predisposing to constipation with a redundant mesocolon may predispose to a volvulus, and acute colonic dilatation may occur spontaneously. A specific problem that may occur in Down syndrome is duodenal atresia/stenosis that may lead to vomiting and intestinal obstruction. In older ages obstruction may also develop if there is foreign body impaction at the site of narrowing.[39] Although it is suggested that certain medications may also effect gut motility and result in obstruction, this has not always been demonstrated.[5,6] Deaths have resulted from untreated Hirshprung disease.[10]

In a study of 27 intellectually-impaired individuals with acute abdomen the two most common problems were volvulus (22.2%) and pseudo-obstruction (18.5%). Upper gastrointestinal haemorrhage occurred in 21 cases, most often due to reflux oesophagitis (62%). The mortality rate following emergency surgery was 21.4%. Reflux oesophagitis is associated with a higher incidence of Barrett oesophagus in this group.[6]

Abnormal eating behaviour is a feature of mental impairment and may result in death from airway obstruction, vascular perforation or gut perforation with sepsis.[40] Patients with pica have an increased rate of hospital admissions with acute abdomen, and also a higher mortality rate, again with volvulus and pseudo-obstruction being the two most common problems.[6] Deaths from malnutrition in Down syndrome were mainly recorded in previous decades and may have been a reflection of poor institutional care or inaccuracy in the diagnosis of the terminal illness. Possible mechanisms of death are summarised in Table 2.

2.5.5. Forensic implications

Individuals with Down syndrome usually have an established diagnosis before they reach the autopsy table. Although this may not be the case in neonates or young infants, the diagnosis is usually not difficult because of the characteristic morphological features, and it can be confirmed by chromosomal studies. Cases of Down syndrome come to forensic attention for a variety of reasons

Table 2
Causes of sudden/unexpected death in Down syndrome

Associated Conditions	
Cardiac	Congenital defects
Respiratory	Upper airway obstruction
	Aspiration
Gastrointestinal	Intestinal obstruction
	Foreign body impaction
Haematologic	Leukaemia
Skeletal	Atlanto-axial instability
Vascular	Pulmonary hypertension
	Fibrointimal hyperplasia
	Pulmonary/coronary artery embolism
Endocrine	Diabetes mellitus
CNS	Dementia
	Seizures
Immunological	Infections
Iatrogenic	Complications of cardiac surgery
Miscellaneous	
Other conditions	
Unrelated natural disease	
Suicide	
Homicide	

including (i) non-specific symptoms and signs with failure to establish a cause of death, (ii) questions regarding the quality of institutionalised care, (iii) the complex nature of underlying conditions and medical treatment, including surgery.

Such cases require careful review of the institution health record including observation charts, staff statements and medication regimes. Discussion with the local children's hospital medical genetics department may be useful as they may have detailed records of previous investigations and assessments. The autopsy should include clear documentation of external and internal features of the syndrome, and any other abnormalities, with photographs and correlation with the clinical record. Any injuries should be carefully assessed and adequate histological sampling of tissues and organs should occur so that an estimation of the length of illness can be made, if required. All major organs and tissues, including bone marrow, should be sampled for microscopic assessment, given the range of congenital and acquired conditions that may manifest in affected individuals. Finally the cause of death should be established and determination should be made as to whether or not the fatal episode was associated with the underlying Down syndrome and its treatment, or was a coincidental event.

References

1. Frid C, Drott P, Lundell B, Rasmussen F, Annerén G. Mortality in Down's syndrome in relation to congenital malformations. *J Intellect Disabil Res* 1999;**43**:234–41.
2. Balarajan R, Donnan SPB, Adelstein AM. Mortality and cause of death in Down's syndrome. *J Epidem Commun Health* 1982;**36**:127–9.
3. Singer RB, Strauss D. Comparative mortality in mentally retarded patients in California, with and without Down's syndrome, 1986–1991. *J Insurance Med* 1997;**29**:172–84.
4. Tolksdorf M, Wiedemann H-R. Clinical aspects of Down's syndrome from infancy to adult life. *Hum Genet Suppl* 1981;**2**:3–31.
5. Jancar J, Speller CJ. Fatal intestinal obstruction in the mentally handicapped. *J Intellect Disabil Res* 1994;**38**:413–22.
6. Khalid K, Al-Salamah SM. Spectrum of general surgical problems in the developmentally disabled adults. *Saudi Med J* 2006;**27**:70–5.
7. Dupont A, Væth M, Vibebech P. Mortality and life expectancy of Down's syndrome in Denmark. *J Ment Defic Res* 1986;**30**:111–20.
8. Baird PA, Sadovnick AD. Causes of death to age 30 in Down syndrome. *Am J Hum Genet* 1988;**43**:239–48.
9. Øster J, Mikkelsen M, Nielsen A. Mortality and life-table in Down's syndrome. *Acta Paediatr Scand* 1975;**64**:322–6.
10. Scholl T, Stein Z, Hansen H. Leukemia and other cancers, anomalies and infections as causes of death in Down's syndrome in the United States during 1976. *Develop Med Child Neurol* 1982;**24**:817–29.
11. Fryers T. Survival in Down's syndrome. *J Ment Defic Res* 1986;**30**:101–10.
12. Hunter AGW. Down syndrome. In: Cassidy SB, Allanson JE, editors. *Management of Genetic Syndromes*. New York: Wiley-Liss; 2001. p. 103–29. Ch. 7.
13. Yang Q, Rasmussen SA, Freidman JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population based study. *Lancet* 2002;**359**:1019–25.
14. Hasle H, Clemmensen IH, Mikkelsen M. Risks of leukaemia and solid tumours in individuals with Down's syndrome. *Lancet* 2000;**355**:165–9.
15. Hermon C, Alberman E, Beral V, Swerdlow AJ. Mortality and cancer incidence in persons with Down's syndrome, their parents and siblings. *Ann Hum Genet* 2001;**65**:167–76.
16. Hill DA, Gridley G, Cnattingius S, Mellemkjaer L, Linet M, Adami H-O, et al. Mortality and cancer incidence among individuals with Down syndrome. *Arch Intern Med* 2003;**163**:705–11.
17. Gatenby P, Tuck R, Andrews C, O'Neil R. Antiphospholipid antibodies and stroke in Down syndrome. *Lupus* 2003;**12**:58–62.
18. Walters RM. Suicidal behaviour in severely mentally handicapped patients. *Brit J Psychiatr* 1990;**157**:444–6.
19. Amanuel B, Byard RW. Accidental asphyxia in bed in severely disabled children. *J Paediatr Child Health* 2000;**36**:66–8.
20. Byard RW. *Sudden Death in Infancy, Childhood and Adolescence*. 2nd ed. Cambridge: Cambridge University Press; 2004.
21. Krous HF, Beckwith JB, Byard RW, Rognum TO, Bajanowski T, et al. Sudden infant death syndrome (SIDS) and unclassified sudden infant deaths (USID): a definitional and diagnostic approach. *Pediatrics* 2004;**114**:234–8.
22. Ogbuihi S, Zink P. Tödliche Lungenblutung bei komplexer pulmonaler Angiodysplasie in einem Fall von Mongolismus. *Z Rechtsmed* 1988;**101**:255–63.
23. Carter G, Jancar J. Sudden death in the mentally handicapped. *Psychol Med* 1984;**14**:691–5.
24. Stahl J, Santos LD, Byard RW. Coronary artery thromboembolism and unexpected death in childhood and adolescence. *J Forensic Sci* 1995;**40**:599–601.
25. Chaney RH, Eyman RK, Miller CR. The relationship of congenital heart disease and respiratory infection mortality in patients with Down's syndrome. *J Ment Defic Res* 1985;**29**:23–7.
26. Chaney RH, Eyman RK, Miller CR. Comparison of respiratory mortality in the profoundly mentally retarded and in the less retarded. *J Ment Defic Res* 1979;**23**:1–7.
27. O'Brien KF, Tate K, Zaharia ES. Mortality in a large southeastern facility for persons with mental retardation. *Am J Ment Retard* 1991;**95**:397–403.
28. Strauss D, Eyman RK. Mortality of people with mental retardation in California with and without Down syndrome, 1986–1991. *Am J Ment Retard* 1996;**100**:643–53.
29. Puri BK, Lekh SK, Langa A, Zaman R, Singh I. Mortality in a hospitalized mentally handicapped population: a 10-year survey. *J Intellect Disabil Res* 1995;**39**:442–6.

30. McKee JR, Bodfish JW. Sudden expected death in epilepsy in adults with mental retardation. *Am J Ment Retard* 2000;**105**:229–35.
31. Hungerford GD, Akkaraju V, Rawe SE, Young GF. Atlanto-occipital and atlanto-axial dislocations with spinal cord compression in Down's syndrome: a case report and review of the literature. *Br J Radiol* 1981;**54**:758–61.
32. Parfenchuck TA, Bertrand SL, Powers MJ, Drvaric DM, Pueschel JM, Roberts JM. Posterior occipitoatlantal hypermobility in Down syndrome: an analysis of 199 patients. *J Pediatr Orthop* 1994;**14**:304–8.
33. Alvarez N, Rubin L. Atlantoaxial instability in adults with Down syndrome: a clinical and radiological survey. *Appl Res Ment Retard* 1986;**7**:67–78.
34. Creutzig U, Ritter J, Vormoor J, Ludwig WD, Niemeyer C, Reinisch I, et al. Myelodysplasia and acute myelogenous leukemia in Down's syndrome. A report of 40 children of the AML-BFM Study Group. *Leukemia* 1996;**10**:1677–86.
35. Rohde M, Banner J, Byard RW. Congenital lesions associated with airway narrowing respiratory distress and unexpected infant and early childhood death. *Forensic Sci Med Pathol* 2005;**1**:91–6.
36. Mitchell RB, Call E, Kelly J. Diagnosis and therapy for airway obstruction in children with Down syndrome. *Arch Otolaryngol Head Neck Surg* 2003;**129**:642–5.
37. Buchin PJ, Levy JS, Schullinger JN. Down's syndrome and the gastrointestinal tract. *J Clin Gastroenterol* 1986;**8**:111–4.
38. Byard RW, Couper RTL. Acute gastric dilatation and spastic quadraparesis. *J Pediatr* 2001;**139**:166.
39. Roy A, Simon GB. Intestinal obstruction as a cause of death in the mentally handicapped. *J Ment Defic Res* 1987;**31**:193–7.
40. Byard RW. Mechanisms of unexpected death in infants and young children following foreign body ingestion. *J Forensic Sci* 1996;**41**: 438–41.